

Appln No. 10/039,952

Reply to Office Action of April 15, 2005

REMARKS/ARGUMENTS

The Office Action dated April 15, 2005, has been reviewed and the comments carefully considered.

Claims 18, 20 and 21 are pending in the application. Claims 18, 20 and 21 are rejected under 35 USC §112 and 35 USC §103, as discussed below.

Claim Rejection Under 35 USC §112

Claim 18, and claims 20 and 21 depending therefrom, are rejected under 35 USC §112 as indefinite. Although Applicant respectfully disagrees that the claims are indefinite, in the interest of expediting prosecution, Claim 18 has been amended.

The Office Action states: "[O]ne would not know if some enzyme has been mutated or not in some fashion, therefor one would not know if the enzyme is encompassed by the claims." Applicant respectfully disagrees. Claim 18 recites "creating a mutated enzyme;" such a mutant enzyme can be synthesized de novo or, alternatively, an existing enzyme can be mutagenized to produce a mutated enzyme having the desired properties. Claim 18 encompasses both scenarios; claim 21, depending from claim 18, encompasses the latter scenario. One synthesizing a protein de novo would clearly know if the enzyme they have produced is a mutant, while one modifying an existing protein would easily be able to determine if the enzyme has been mutated by comparing its activity to the existing enzyme, as described in the Specification (see, e.g., pages 4-5 of the Specification). From the language of claim 18, it would be clear to one of skill in the art that so long as one creates an enzyme that reductively aminates a ketone that is not a 2-ketoacid, to produce an amine that is not an alpha-amino acid, either de novo or through mutagenesis of an existing enzyme, such that the mutated enzyme reductively aminates at a greater rate than the existing enzyme, that created enzyme will fall within the scope of the claim.

Claim Rejection Under 35 USC §103

In order to establish a prima facie case of obviousness, three requirements must be satisfied. First, there must be some suggestion or motivation in the prior art relied upon to modify the reference. See *In re Fine*, 837 F2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir.

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1988). Second, there must have been a reasonable expectation of success for the proposed modification, at the time the invention was made. See *Amgen, Inc. v. Chugai Pharm. Co.*, 927 F2d 1200, 1209, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Third, the prior art reference must teach or suggest all the limitations of the claims. See *In re Wilson*, 424 F2d 1382, 1385, 165 USPQ 494, 496 (C.C.P.A. 1970).

Applicant respectfully submits that the Office Action fails to make a prima facie case of obviousness, as the prior art references do not teach or suggest all the limitations of claim 18, the sole independent claim.

Claim 18, as amended, provides (emphasis added):

A method for producing an amine from a target ketone, comprising:
creating a mutated enzyme that catalyzes reductive amination of the target ketone; and
providing the mutated enzyme in a reaction mixture comprising the target ketone under conditions sufficient to permit the formation of the corresponding amine to thereby produce the amine,
wherein the ketone is not a 2-ketoacid and the amine is not an alpha-amino acid.

Applicant respectfully submits that the Office action points to no teaching or suggestion in any of the cited references for a method for producing an amine that is not an alpha-amino acid by reductively aminating a ketone that is not a 2-ketoacid using a mutated enzyme.

Yamada (US 2002/0192786 A1) is cited for teaching "enzymes that act on a ketone compound in the presence of an amino group acceptor" (citing Table 3 on page 5) as well as "methods of isolating various enzymes." However, these enzymes are all transaminases (see Yamada, para. 0063, and Table 3), not mutant reductive aminases as recited in claim 18 and the claims depending therefrom.

Liu (U.S. Pat. No. 6,365,380) is cited for teaching "amino acid transaminases where keto groups are converted to amines" and notes that in claim 1 "amino acid dehydrogenase is shown." As with Yamada, the Office action points to no teaching or suggestion in Liu for

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using mutant enzymes to produce an amine that is not an alpha-amino acid from a ketone that is not a 2-ketoacid. Moreover, Liu's use of amino acid dehydrogenase for converting a 2-ketoacid to an alpha-amino acid is quite different from Applicant's enzymatic method of producing a ketone that is not 2-ketoacid from an amine that is not an alpha-amino acid, a method which is described for the first time in the Instant Application.

Engel is cited for teaching "modifying enzymes" and "modified amino acid dehydrogenases." Nowhere, however, does the Office action point to a teaching or suggestion to modify amino acid dehydrogenases (or any enzyme that reductively aminates) for the conversion of a ketone that is not 2-ketoacid to an amine that is not an alpha-amino acid.

Yan is cited for teaching "mutants of dehydrogenases." Applicant notes that the dehydrogenases described in Yan are alcohol dehydrogenases, not amino dehydrogenases. Moreover, as with the other cited references, Yan provides no motivation or teaching for making mutants for the purpose of reductively aminating ketones that are not 2-ketoacids.

Claims 20 and 21 depend, directly or indirectly from claim 18, and are submitted to be allowable as dependent upon an allowable base claim, and for the additional limitations recited therein.

Applicant respectfully submits that the Instant Application is the first disclosure of a method for using mutated enzymes to produce amines that are not alpha-amino acids from ketones that are not 2-ketoacids by reductive amination.

In view of the foregoing amendment and response, it is believed that the application is in condition for allowance and, accordingly, reconsideration and allowance is earnestly solicited.

If any questions remain regarding the allowability of the application, Applicant would appreciate if the Examiner would advise the undersigned by telephone.

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The Commissioner is hereby authorized to charge any fees under 37 CFR 1.16 and 1.17 which may be required by this paper to Deposit Account No. 03-1728. Please show our docket number with any charge or credit to our Deposit Account.

Respectfully submitted,
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